PREVENTION OF BISPHENOL AN INDUCED HISTOPATHOLOGICAL INSULTS TO URINARY CORPUSCLE OF ALBINO RAT KIDNEYS BY MORINGA OLEIFERA

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ABSTRACT

Background: The use of medicinal herbs has been in practice in our society since ages. Similarly, with the evolution of plastics, the use of plastic ware has increased in the past few decades. Along with other injurious substances, it contains Bisphenol A, that is a known deleterious agent for human health. Now a day's modern medicine has evolutionized and taking refuge in using herbal substances in preparing allopathic medicines too. One such medicinal plant being studied far and wide for its excellent antioxidant properties is Moringa oleifera.

Objectives: To prevent Bisphenol A induced histopathological insults to urinary corpuscle of albino rat kidneys by Moringa oleifera.

Methods: A total of 30 adult albino rats of either gender were taken and made three groups A, B and C each of which contained 10 rats. The group A, was control. The group B, BPA-exposed, was ingested with 50mg/kg of BPA. The third group, C, was simultaneously administered 400mg/kg MoLE along with 50 mg/kg BPA. Rat kidney specimens were histologically evaluated by hematoxylin and eosin staining. The experimentation took total eight weeks investigated the probable efficacies of leaves of Moringa Oleifera in comparison to histo-pathological alterations in the renal corpuscles of albino rats induced by BPA.

Results: BPA exposure resulted in renal corpuscle damage in the rat kidneys as evident via increased urinary space diameters along with glomerular congestion noticed in the group B. However, rats getting MoLE indicated notable absence of these histopathological alterations. This shielding provided by MoLE against BPA may be credited to its nutritiously active contents like polyphenols and flavonoids, which fight oxidative injuries as well as inflammation.

Conclusion: This study guides us into the large number of medicinal benefits of Moringa plant including its role in prevention of oxidative injuries being caused by toxins like BPA to renal corpuscles in rat kidneys.

Keywords: BISPHENOL A (BPA), Glomerulus, Kidneys, Moringa Oleifera leaves extract (MoLE), Renal corpuscle, Urinary space.

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INTRODUCTION

Bisphenol A, an estrogenic-compound that is known to be a part of plastic ware, inner tin can linings as well as epoxy resins.[1] It has fungicidal properties too and even very low doses have been established to be injurious to the human health especially the kidneys.[2] Studies reported previously that BPA exposure to experimental animals resulted in clear histopathological damage to renal system especially the kidneys.[3]

The renal corpuscle is a pivotal piece of the kidney's architecture as well as physiology. And is responsible for initiating the filtration of blood to form urine. It contains two master components**,** glomerulus along with the Bowman's capsule. Glomerulus is a cluster of tiny blood vessels (capillaries) where blood is filtered and Bowman's capsule has a cup-like appearance that surrounds the glomerulus, collecting the filtrate.[4]

The **urinary space** (also known as the **Bowman's space)** is the space within the visceral and parietal layers lining the Bowman's capsule. And is the area where the filtrate from the blood, which has been processed through the glomerulus, collects before moving into the proximal convoluted tubule for further processing. [5]

BPA is known to be nephrotoxic and also results in glomerular injuries. Role of renal corpuscle is crucial to the human renal function. Hence oxidative stress causing substances, like BPA may result in a decline in renal function.[6] This has been reinforced previously by avast variety of data seen in the several studies showing injury to proximal and distal tubules, glomerular congestion, inflammatory interstitial infiltrates and vascular congestion in renal parenchyma.[7]

Moringa Oleifera is taken to be a tree full of miracles. Its use is well established for various human ailments including cancers, tumors, nutrition supplement, anti-inflammatory and a powerful anti-oxidant.[8] Every constituent of Moringa tree including seeds to shoots to leaves and flowers have separate benefits. Its leaves are loaded with various vitamins along with minerals (iron, calcium), and are often used in salads, soups, and teas. They can be dried and powdered for use as a dietary supplement.[9]

Owing to presence of anti-oxidants like tocopherols, flavonoids, **quercetin, chlorogenic acid, catechins, beta-carotene** and vitamins along with minerals[10], Mo has protective properties against toxins that include BPA as well.[11] Rationale for selecting Mo to counter balance deleterious effects of BPA on rat kidneys is also because of its rich medicinal constituents.

Thus, acknowledging, the potential of Moringa Oleifera to fight oxidative injuries, this study looks forward to deduce the probable sheltering provided by the extract of Moringa Oleifera (MoLE) against histopathological transformations caused to renal corpuscles of adult albino rat kidneys being attacked by BPA. By clarifying impact of MoLE on histopathology induced by BPA on urinary corpuscles of albino rat kidneys, the aim is to provide some innovative ideas into the therapeutic fields for using natural herbs of medicinal importance that could protect our kidneys against environmental pollutants.

METHODS

Experimental research was carried out at Animal house including Histology laboratory of Postgraduate Medical Institute (PGMI), Lahore. The study protocol was agreed upon by Advanced Studies and Research Board of University of Health Sciences, Lahore, and Ethical Committee of PGMI. The study trial included 30 adult albino rats of male/female gender and weighing 160-180 grams. Total duration including experiment, data analysis and interpretation took almost 12 months including 8 weeks experimentation duration. Rats not fulfilling inclusion criteria as well as diseased or pregnant rats were excluded. A sample size of 30 rats (albino) was taken having a significance level of 5% carrying a Power of the study of 90%, a sample size in every group (total groups = 3) was taken to be 10, to make a total sample size of 30.

Animals for this research were acquired from National Institute of Health, Islamabad. All the animals were reviewed keenly before the experiment was initiated. Males and females were housed separately in a climate-controlled environment and treated in accordance with the principles and guidelines for care and use of experimental animals in research as promoted by the Canadian Council of Animal care [12]. Room in which they were placed was well ventilated, at ambient temperature of 28.0±2.0ºC and humidity (60±10%) under 12 hr light/dark cycles and well provided with standard rat diet and water *ad libitum.*

Following acclimatization for a period of one week, the procedure was started. 30 rats were assigned randomly as 1,2,3,4... Each animal was labeled according to groups and weighed before the start of the study. Weight was recorded on an electronic scale (Sartorius Precision Balance, Germany)

Table 1: Showing detail of the Animal Groups and Experimental Intervention.

Group n = 10	Administration	Week of Sacrifice	Intervention and Dosage
A Control	Orally	End of 8 week	1ml/kg distilled water only
B Experimental			BPA 50 mg/kg suspended in distilled water
C Experimental			BPA 50 mg/kg + *MoLE* 500 mg/kg dissolved in distilled water

n = Number of rats in each group.

BPA and *MoLE* were administered through oral gavage

Duration of experiment was eight weeks. All rats were sacrificed after completion of eight weeks.

Procurement of BPA and Moringa oleifera Leaves: Source of BPA was DAEJUNG (Korea), provided in the form of crystals that were white. ADNF electronic balance was used to weigh it, mortar and pestle used for grinding while distilled water used to make its suspension.

Moringa oleifera leaves were obtained from botanical garden located in University of the Punjab, Lahore, Pakistan. Leaves were authenticated by Professor Abdul Nasir Khalid, Department of Botany, University of the Punjab. A voucher specimen of no LAH35146 was kept in herbarium for future reference.

Preparation of Dose: Dose was freshly prepared on daily basis accordingly standard methods and calculated accordingly body weight.

Dissection Method: Animals were sacrificed after 24 hours of administration of the last dose at end of the 8th week.

Histological Parameters:

Hematoxylin and Eosin Stain:

Sections of kidney were stained and then visualized under the light microscope, using different magnifications (10X, 20X and 40X) to notice histological alterations. Comparison amongst control and experimental groups was done on the basis of the following parameters.

Renal Corpuscle:

Quantitative: Urinary space (µm)

Qualitative: Glomerular vascular congestion (present/absent)

Width of the urinary/glomerular space: Urinary spaces measurements were taken at 40X. For each slide, three randomly selected different fields were observed. From each field, the width of three intact urinary spaces was determined from three areas; cortical, mid cortical and juxta medullary. Mean size was calculated by the ending time.

RESULTS

Glomerular Space: The mean of glomerular space in all trial groups was calculated. To compare the glomerular space among groups, one-way ANOVA test was made use of. Comparison showed that the mean glomerular space in all of the groups were significantly different (p-value < 0.001) (Table 2).

Table 2: Comparison of glomerular space among groups

Parameters	Group A	Group B	Group C	p-value
Glomerular space	7.68 ± 0.47	12.72 ± 0.61	8.25 ± 0.56	< 0.001*

One way ANOVA

*p value ≤ 0.05 is considered statistically significant

For making multiple comparisons, post hoc Tukey test was implied which narrated that glomerular space in group B was significantly higher as compared to group A along with C. On the contrary, significant difference was not found in the glomerular spaces of groups A as well as C (Table 3).

Table 3: Pair wise comparison of glomerular space among groups

	Multiple Comparison					
	S. No.	Groups (I)	Groups (J)	Mean Difference (I-J)	Std. Error	p-value
Glomerular space	1	A	B	-5.0400*	.24460	0.000
			C	-0.5700	.24460	0.069
	2	B	C	4.4700*	.24460	0.000

*p value ≤ 0.05 is considered statistically significant

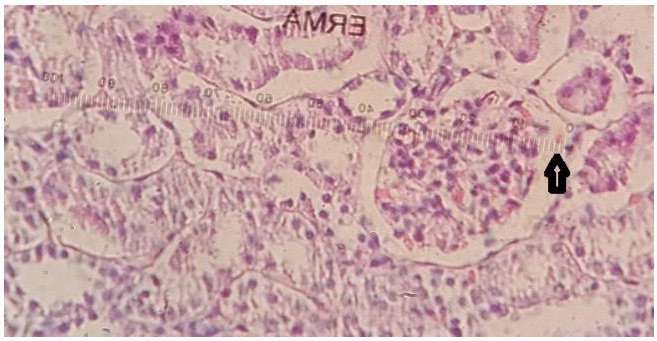

Fig. No. 1: Photomicrograph of the kidney showing measurement of urinary space (black arrow) as seen through a microscope.

VASCULAR CONGESTION

An association was illustrated by Fisher's exact test between Glomerular vascular congestion and groups. Vascular congestion in glomeruli in all rats of control group A was not present. In group named B, it could be micro scoped in kidney glomeruli of all rats where as in group named C, it was shown by kidneys of only 2 (20.0%) rats (Table. 4).

Table 4: Distribution of Glomerular vascular congestion among groups

Vascular Congestion	Group A n (%)	Group B n (%)	Group C n (%)	p-value
Present	0 (0.0%)	10(0.0%)	2 (20.0%)	< 0.001*
Absent	10 (100.0%)	0(0.0%)	8 (80.0%)	

Fisher's exact test

*p value ≤ 0.05 is considered statistically significant

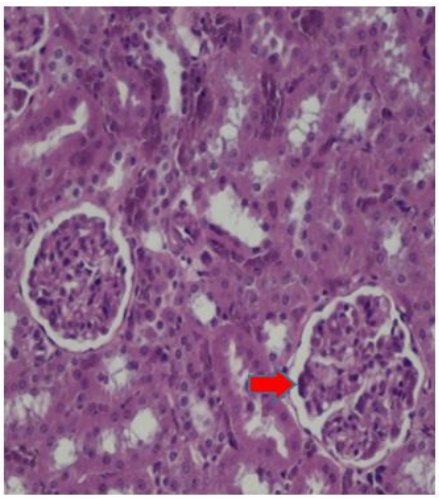

Fig. no. 2a. red arrow shows normal glomerulus in group A.

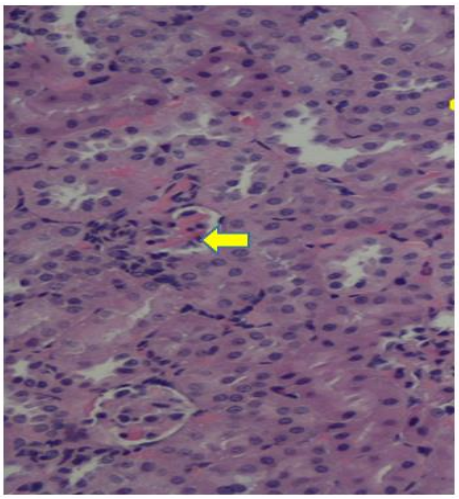

Fig. no. 2b. yellow arrow shows glomerular vascular congestion in group B**.**

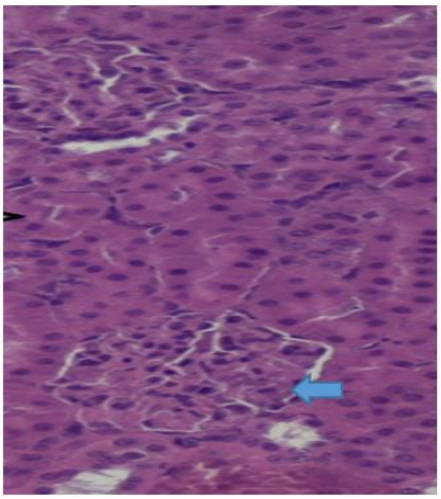

Fig. no. 2c. blue arrow shows normal glomerulus in group C.

DISCUSSION

As the age of modernization continues, so do the enhancements in the technology and human inventions including diversity in plasticizing industry. An unfortunate consequence of which is a huge increase in environmental and human health hazards. BPA is one of such man-made chemical substance that is frequently used in plastic bottles including baby feeders as well as other plastic objects.[13]

BPA has been implied in causing oxidative injuries to rat kidneys including nephrons, interstitium as well as glomeruli in a dose dependent manner.[14] Hence it was chosen to injure the renal cytoarchitecture in the experimental albino rats as was evident through previous trials (fig. no. 2b.).[15]

Moringa oleifera (Mo) is an antioxidant proven to be a medicinal plant and has nephron- protective effect in several experimental models majorly due to its highly bio active compound composition.[16]

The study interpreted the shielding effect of MoLE in the renal corpuscles of the BPA injured rats. The urinary spaces diameters in the BPA exposed groups were deemed to be greater [17] as compared to that of the group that was simultaneously administered MoLE, showing preventive as well as protective efficacy of the later in accordance to the experiments done earlier.[18] More over presence or absence of glomerular congestion was also examined and found to be positive for BPA exposed rats and no or least congestion in MoLE supplemented ones (fig. no. 2 a, b, c).[19] Similarly, another study conducted remotely suggested glomerular damage including congestion of vessels as well as disrupted Bowman's capsular epithelium of the rat kidneys with oral exposure to BPA.[20]

The dose related increase in the width of glomerular space was concluded by BPA exposure. The glomerular space might be widened due to the necrosis of cells lining glomerular capsule causing glomerular shrinkage. This might have occurred as a consequence of metabolites of BPA and inefficiency of the rat kidneys to extrude those causing necrosis and degeneration of renal tubules. [21]

On the other hand, many former experimentations regarding nephron protective role and activity of Mo against various nephron toxic substances including various medicines as well as oxidative insults inflicting agents like BPA, had proven to be true.[22] Experiments tested and stated that Mo reacts with and ends up reactive oxygen species and lipid peroxidation in renal tissues and restores depleted glutathione after toxic drug administration. Mo seed and leaves contain many reactive substrates as glucosinolates, isothiocyanates, thiocarbamates and flavonoids which enhance its antioxidant activity.[23]

Another convincing recent research demonstrated that BPA inflicted renal injuries on albino rats kidneys were treated by giving various (100 mg/kg, 200 mg/kg, 300 mg/kg, 400 mg/kg) doses of moringa oleifera and seen to be curative.[24]

CONCLUSION

Moringa Oleifera leaves extract proved to be helpful in preventing BPA induced injury to renal corpuscle in the kidneys of adult albino rats.

LIMITATIONS: Since this study's experimentation interval consisted of a short duration of eight weeks, the results need to be tested for a longer period of time.
As the study included only Male rats due to possible hormonal issues related to female rats, so, female rats might be included in the study to establish sex specific effects.
Moreover, the study was conducted on rat models, human studies must be looked into for establishing more human specified trials.

ETHICAL APPROVAL

Ethical approval of synopsis was granted by the Institutional Ethical Committee of AMC/PGMI/LGH;

CONFLICT OF INTEREST:

Authors declare no conflict of interest.

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AUTHOR'S CONTRIBUTIONS

RE: Concept, manuscript writing
HF: Manuscript writing, data analysis
MS: Manuscript writing, data collection
AS: Data collection, Data analysis
KS, AM: Data analysis, literature review
All Authors: Approval of the final version of the manuscript to be published

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